80. An agent for treating pain comprising a botulinum toxin serotype A covalently coupled to substance P, wherein an H_c of the toxin has been removed, the agent treats pain by acting on the projection neuron.

Support for the Amendments:

Support for the amendments to the claims may be found in the specification as filed. For example, support may be found at least at page 23, lines 7-29.

Remarks

Item 1 of the Office Action - Status of the Claims

By way of this Response, claims 66-68 have been canceled, and claims 69-73, 77, and 78 have been amended. Accordingly, claims 69-80 are pending.

Items 2-5 of the Office Action - Rejections Withdrawn

Applicant acknowledges that the previous rejections of the claims under 35 U.S.C. §§ 112 and 102 have been withdrawn. Applicant also acknowledges that claims 66-80 are free from the art.

Item 6 of the Office Action - Rejections Under 35 U.S.C. § 112, First Paragraph

In the July 11, 2001 Final Office Action, the Examiner has rejected claims 67 and 68 under 35 U.S.C. § 112, first paragraph as allegedly not enabled by the specification of the application.

Applicant respectfully disagrees, but in order to move the prosecution of this case forward, Applicant has canceled claims 67 and 68. Therefore, the rejection of those claims is rendered moot.

Item 7 of the Office Action - Rejections Under 35 U.S.C. § 112, Second Paragraph

In the July 11, 2001 Final Office Action, the Examiner has rejected claims 66-68 as allegedly indefinite.

Applicant respectfully disagrees, but in order to move the prosecution of this case forward, Applicant has canceled claims 66-68. The rejection is rendered moot.

Item 10 of the Office Action - Allowed Claims

In the July 11, 2001 Final Office Action, the Examiner has indicated that claims 69-80 appear allowable. During a telephone conversation with the undersigned on December 21, 2001, after the mailing of the Advisory Action, the Examiner told Dr. Hollrigel that she has a concern regarding claims 69-80, in particular, she has concern that at least some of the claims (e.g., claim 69) encompassed an agent having multiple functional targeting moieties, such as a Clostridial neurotoxin having a functional H_c domain and substance P attached to the neurotoxin.

To address and remove the Examiner's concerns, Applicant has amended the independent claims to reflect that the agent of the invention does not have a functional H_c. In other words, the claims now recite an agent for treating pain that has a substance P targeting moiety instead of the native targeting moiety of the neurotoxin. Accordingly, the agent recited in the claims lacks an H_c that binds to native neurotoxin receptors at the n uromuscular junction with the same affinity as native neurotoxins. Thus, the claims encompass modifi d neurotoxins that have had at least a portion of the

H_c removed or modified so that the neurotoxin no longer binds to native neurotoxin receptors at the neuromuscular junction with the same affinity as unmodified neurotoxins. Applicant respectfully submits that such an amendment is clearly sufficient to address and remove the Examiner's concerns.

In view of the foregoing amendments and remarks, Applicant respectfully submits that the claims are not disclosed or suggested by the prior art, and respectfully submits that the claims are in condition for allowance. Notice of which is respectfully requested.

If a telephone interview would be of assistance in advancing prosecution of the subject application, Applicant's undersigned representative invites the Examiner to telephone Dr. Hollrigel at the number provided below.

Date: 1/15/02

Respectfully submitted,

Frank J. Uxa
Attorney for Applicant
Registration No. 25,612
4 Venture, Suite 300
Irvine, California 92618
(949) 450-1750
(949) 450-1764 Facsimile

CERTIFICATE OF FACSIMILE TRANSMISSION
I hereby certify that this correspondence is being transmitted via facsimile to the Commissioner for Patents in Washington, DC 20231, to fax number 703-308-0294, on or before January 15, 2002

Jean F. Heuler

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

Claims 66-68 have been canceled without prejudice.

Claims 69-80 have been amended as follows:

69. (Amended) An agent for treating pain comprising a modified clostridial neurotoxin, wherein the clostridial neurotoxin has been modified by ~~component~~ covalently coupling ~~ed to~~ substance P to the clostridial neurotoxin so that the clostridial neurotoxin no longer binds to neurotoxin receptors at a neuromuscular junction with the same affinity as a native clostridial neurotoxin.

70. (Amended) The agent of claim 69 wherein the clostridial neurotoxin ~~component~~ is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum and Clostridial tetani.

71. (Amended) ~~An~~ The agent of claim 69 wherein the clostridial neurotoxin ~~component~~ is a botulinum toxin selected from the group consisting of serotype A, serotype B, serotype C_1, serotype D, serotype E, serotype F and serotype G.

72. (Amended) The agent of claim 69 wherein the clostridial neurotoxin ~~component~~ is botulinum toxin serotype A.

73. (Amended) The agent of claim 69 wherein the clostridial neurotoxin ~~component~~ comprises an H_N and an L chain.

74. The agent of claim 73 wherein the H_N is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum and Clostridial tetani.

75. The agent of claim 73 wherein the L chain is produced by an organism selected from the group consisting of Clostridial beratti, Clostridial butyricum, Clostridial botulinum, and Clostridial tetani.

76. The agent of claim 73 wherein the H_N is obtained from a botulinum toxin selected from the group consisting of botulinum toxin serotype A, serotype B, serotype C_1, serotype D, serotype E, serotype F and serotype G.

77. (Amended) An agent for treating pain comprising a botulinum toxin, without an H_c that binds to receptors at the neuromuscular junction with the same affinity as native botulinum toxin, covalently coupled to substance P.

78. (Amended) An agent for treating pain comprising a botulinum toxin serotype A, without a functional H_c domain, covalently coupled to substance P.

79. An agent for treating pain comprising a botulinum toxin covalently coupled to substance P, wherein an H_c of the toxin has been removed.

80. An agent for treating pain comprising a botulinum toxin serotype A covalently coupled to substance P, wherein an H_c of the toxin has been removed, the agent treats pain by acting on the projection neuron.